Original Article

Effectiveness of platelet rich fibrin versus demineralized bone xenograft in periodontally accelerated osteogenic orthodontics: *A pilot comparative clinical study*

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ABSTRACT

Objectives: To compare the rate of extraction space closure between periodontally accelerated osteogenic orthodontics (PAOO) using platelet-rich fibrin (PRF) (Group 1) and PAOO using demineralized bone xenograft (DMBM) (Group 2) and to compare the level of wound healing between the PRF group vs the DMBM group after PAOO.

Materials and Methods: A two-arm prospective single blind pilot study with a split-mouth design was used in which 14 patients requiring premolar extraction were divided into two groups: PRF and DMBM. En-masse space closure was carried out with using mini implants after the PAOO procedure. The amount of space closure was measured at five time points with 2-week intervals within 2 months. The gingival healing levels were assessed using early wound healing scores on the first postoperative day.

Results: The rate of extraction space closure was faster in the experimental quadrant at all time points (T1-T4) in the PRF group and at time points (T3, T4) in the DMBM group. Comparison between experimental quadrants showed a significant increase in the rate of space closure in the PRF group T1 to T3 ($P < .05$). The PRF group showed higher total early healing scores than the DMBM group.

Conclusions: PRF, when used in the PAOO procedure, produces a faster rate of space closure with better early wound healing than DMBM. (*Angle Orthod.* 2022;92:180–188.)

KEY WORDS: Platelet rich fibrin; Periodontally accelerated osteogenic orthodontics; DMBM

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INTRODUCTION

The development of corticotomy-assisted orthodontic treatment (CAOT) opened new frontiers for addressing many limitations in the orthodontic treatment of adults. Alveolar decortication with an augmentation bone grafting technique, when combined with orthodontics, is called periodontally accelerated osteogenic orthodontics or PAOO and was first described in 2001.[1] PAOO has shown to provide an increased net alveolar volume after orthodontic treatment. It is a combination of selective decortication facilitated orthodontics and alveolar augmentation. The several advantages of the PAOO protocol include reduced treatment time, enhanced expansion, differential tooth movement, increased traction of impacted teeth and more post-orthodontic stability.[2–4]

The graft-assisted PAOO procedure extends the limits of tooth movement and orthodontic treatment. In cases where it is not possible to achieve ideal occlusion, acceptable stability, normal function, and

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optimal facial balance with conventional orthodontic therapy, PAOO may offer a viable alternative.[5] The success of the PAOO technique depends on the effectiveness of the surgical technique and the periodontal healing process. The rate and outcome of gingival and periodontal structure healing determines the force that can be applied for achieving rapid tooth movement. Wilcko et al., in their PAOO protocol, advocated the use of particulate bone graft material such as deproteinized bovine or autogenous bone, decalcified freeze-dried bone allograft or a combination, over decorticated alveolar bone.[6]

The potential of autologous graft materials such as platelet-rich fibrin (PRF) and platelet-rich plasma (PRP) in oral tissue regeneration has accentuated their importance in clinical dentistry, implantology, and PAOO in particular. The advantages of PRF over PRP include easier manipulation, cost effectiveness, no biochemical handling of patient blood samples, relatively better wound healing potential due to a lower degree of polymerization, and absence of bovine thrombin and anticoagulants that enable tissue regeneration.[7–11] PRF is also reported to reduce patient discomfort during the early period of wound healing due to the release of various growth factors such as platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and vascular endothelial-derived growth factor (VEDGF).

The centrifuge speed used determines the types of PRF classified as P-PRF (pure platelet rich fibrin) and L-PRF (leukocyte-platelet-rich fibrin). Choukroun recently reported A-PRF (advanced PRF), i-PRF (injectable PRF), and liquid PRF based on the centrifuging time. i-PRF is a platelet concentrate in liquid form that can be polymerized with bone graft xenograft and is known as sticky bone (sticky PRF), an emerging trend that has gained applications in periodontology and implantology.[12–14] There is a paucity of data on the possibility of incorporating L-PRF in PAOO toward achieving a better surgical outcome and healing and the graft materials used in PAOO have not been compared.[15–17]

The aim of this pilot study was to compare the effectiveness of PRF vs demineralized bone xenograft (DMBM) in affecting the rate of space closure and early wound healing in the PAOO procedure.

MATERIALS AND METHODS

The study was initiated after obtaining Institutional ethics committee approval (IGIDSIEC2018NRP18-FAAYOPO) at Indira Gandhi Institute of Dental Sciences, Sri Balaji Vidyapeeth Deemed to be University, Puducherry, India. The study design for this pilot trial was a prospective, split mouth, double-arm clinical trial.

The inclusion criteria were as follows: (1) Patients with Angle Class I malocclusion with anterior crowding (greater than 5 mm) or bimaxillary protrusion requiring extraction of premolars; (2) Patients diagnosed with Angle Class II, division 1 malocclusion requiring extraction of first premolars (maximum anchorage); (3) Patients with healthy periodontal status willing to undergo the PAOO procedure and; (4) Patients who were above 18 years of age and below 40 years of age.

The exclusion criteria in this study were: (1) Patients with a skeletal Class III base or with dentofacial deformities, endodontically or prosthodontically treated or malformed canines; (2) Patients with active periodontal disease or very poor oral hygiene; (3) Patients with debilitating diseases or systemic illness; (4) Patients for whom lower second premolar extraction was planned as a part of Class II correction.

Thirty-two patients who met the inclusion criteria were selected, out of which 14 patients agreed to participate. The other patients either dropped out during the alignment and leveling stage or were apprehensive about the invasiveness of the PAOO surgical techniques. The patients were allocated into two groups: the PRF group (Group 1; Split mouth with conventional retraction mechanics for one quadrant and PAOO with PRF for the contralateral quadrant) and the DMBM group (Group 2; Split mouth with conventional retraction mechanics for one quadrant and PAOO with DMBM for the contralateral quadrant).

Each patient signed informed consent after receiving a thorough explanation and information sheet regarding the study. The protocol was explained in detail about the PAOO procedure with PRF and PAOO with DMBM. An information sheet regarding the PAOO procedure, its proposed advantages including any risks associated, were provided in English and vernacular language and explained by the principal investigator. The values of mean space closure velocity from the study by Al-Naoum et al.[4] was used in calculation of the sample size for this pilot trial.

Bonding of fixed orthodontic appliances (MBT 022″ slot) was carried out within one week of extraction of premolars. After a minimum of 5 months after bonding, at the start of retraction, patients who were willing to undergo PAOO therapy were allocated to the PRF group (PRF assisted PAOO) or the DMBM group (DMBM assisted PAOO). 4 weeks before PAOO, inter radicular mini implants of 1.4×8 mm dimension were loaded between the 2nd premolar and 1st molar of both the control and experimental quadrant. The graft material, either PRF or DMBM was based on the patient's choice. Many of the patients remained

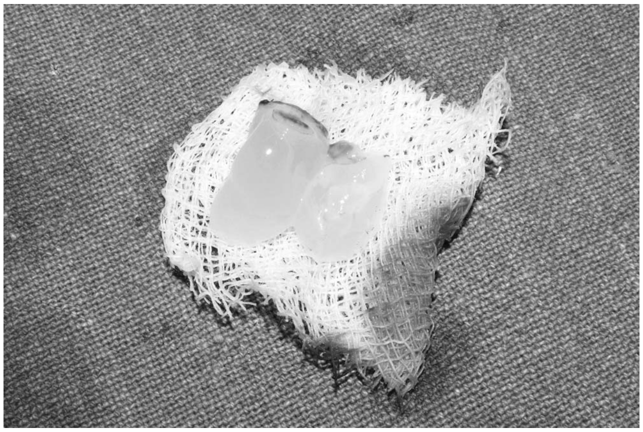

Figure 1. PRF prior to placement.

apprehensive regarding the procedures involved in PRF preparation and, hence, randomization was not possible.

The surgical procedures related to PAOO were performed under the supervision of the co-investigators of this study. To reduce the risk of bias, the assessment of rate of space closure and level of wound healing was done by a different assessor unrelated to the study. The PAOO procedure performed is detailed as follows:

Group 1: (PAOO Using PRF)

PRF preparation. Peripheral blood samples were collected into 10-mL glass-coated tubes without anticoagulants for centrifuging at 3000 revolutions per minute for 10 minutes according to the protocol developed by Choukroun et al.[8,9] Clots were then carefully separated from red blood cell precipitants (Figure 1).

Incorporation of PRF. A modified "Wilcko" technique incorporating the use of L-PRF as grafting material under antibiotic coverage was used in the experimental

Figure 2. Flap elevation.

Figure 3. Corticotomy cut.

quadrant. After administration of local anesthesia, a full-thickness envelope flap was raised preserving the interdental papillae (Figure 2). Vertical corticotomy patterns were performed using either rotary or piezoelectric instruments. Cuts that extended from 2 mm below the bone crest penetrating 1.5 to 2 mm into the cortical plate until reaching the cancellous bone were placed. Also, 2-mm bur holes were also placed at the site (Figure 3). After controlling the bleeding, minced pieces of L-PRF were placed on the corticotomy site (Figure 4) and resorbable sutures were placed along the vertical incisions.

Group 2: PAOO Using DMBM

"Wilcko" technique with DMBM as grafting material with antibiotic treatment was administered in the experimental quadrant. The same surgical procedures mentioned already were followed. After controlling the bleeding, DMBM (Osseograft Advanced Biotech Products (P) Ltd,India) 0.5 cc was placed on the corticotomy site (Figure 5) and resorbable sutures were placed.

Figure 4. PRF placed at corticotomy site.

Figure 5. DMBM over corticotomy site.

Space closure was achieved on 0.017 $\times$ 0.025-inch stainless steel orthodontic wire using elastomeric chain from the mini implant to the power arm of a sliding hook, thereby using direct anchorage (Figure 6). The force required (200 grams/quadrant) was calibrated using a Dontrix gauge (JJ Orthodontics, India).

The amount of extraction space (distance between the distal surface of the canine to the mesial surface of the premolar) was measured to an accuracy of 0.05 mm using digital calipers and recorded by an independent assessor. The amount of extraction space was evaluated at five time points (T0 to T4). In patients for whom the mini implants loosened, the measurements were taken after replacement of the mini implants. The difference between each consequent time point was 2 weeks. The final time point was taken as the amount of space closure at the 12th week (Table 1).

Comparative objective assessment of early wound healing was done between the PRF group and the DMBM group patients after PAOO. Patients were recalled 24 hours after surgery and a trained examiner who was not part of the study assessed early wound healing using the EHS early wound healing score.[18]

Figure 6. Mini implant-assisted space closure.

Table 1. Measurement of Amount of Space Closure at Various Time Points (T0 to T4)

S No.	Time Interval	Measurement	Description[a]
1	T0	Distance between mesial surface of premolar to distal surface of canine (in mm)	2 wk after PAOO (start of retraction)
2	T1	Distance between mesial surface of premolar to distal surface of canine (in mm)	4 wk after PAOO
3	T2	Distance between mesial surface of premolar to distal surface of canine (in mm)	6 wk after PAOO
4	T3	Distance between mesial surface of premolar to distal surface of canine (in mm)	8 wk after PAOO
5	T4	Distance between mesial surface of premolar to distal surface of canine (in mm)	10 wk after PAOO

[a] PAOO indicates periodontally accelerated osteogenic orthodontics.

Only the vertical releasing incisions were assessed (Table 2).

RESULTS

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 (version III, SPSS Inc., Chicago) for Windows. Paired *t*-tests were used to determine the significance of differences between the experimental and control quadrants for the PRF group and the DMBM group. An independent sample *t*-test was used to compare the experimental quadrants of the PRF group vs the DMBM group. Comparison of the EHS scores (clinical signs of re-epithelialization or CSR, clinical signs of hemostasis or CSH, clinical signs of inflammation or CSI, and Total scores) between the PRF group and the DMBM group was analyzed by Mann-Whitney *U*-test.

Table 2. EHS Description According to Lorenzo Marini et al[11,a]

Parameter	Description	Points
CSR	Grading based on merging of incision margins	6 or 3 or 0
CSH	Signs of haemostasis such fibrin at incision margins/bleeding	2 or 1 or 0
CSI	Grading based on redness along length of incision	2 or 1 or 0
Maximum total score: 10		

[a] CSH indicates clinical signs of hemostasis; CSI, clinical signs of inflammation; CSR, clinical signs of re-epithelialization; EHS, early wound healing score.

Table 3. Descriptive Statistics for Amount of Extraction Space in Control and Experimental Quadrants in Group 1 (PAOO Using PRF) and Group 2 (PAOO Using DMBM) at different time points (T0 to T4)[a]

	N	Minimum	Maximum	Mean	SD	*P* Value
Control quadrant						
1						<.001
T0	7	4.0	8.0	6.26	1.61	
T1	7	3.0	8.0	5.50	1.83	
T2	7	2.5	7.0	4.81	1.75	
T3	7	2.0	6.0	4.14	1.65	
T4	6	1.5	5.0	3.35	1.51	
2						<.001
T0	7	3.0	8.0	5.57	1.90	
T1	7	2.0	7.5	4.81	1.98	
T2	7	2.0	6.5	4.57	1.86	
T3	6	1.5	6.0	4.42	1.56	
T4	6	1.0	5.5	4.00	1.58	
Experimental quadrant						
1						<.001
T0	7	4.00	9.00	6.21	1.82	
T1	7	2.50	7.00	4.64	1.82	
T2	7	1.20	5.50	3.53	1.87	
T3	7	0.50	4.50	2.40	1.62	
T4	6	0.00	2.90	1.13	1.27	
2						<.001
T0	7	4.00	8.00	5.96	1.39	
T1	7	3.80	6.50	4.70	1.07	
T2	7	2.50	4.80	3.51	0.95	
T3	6	1.70	3.70	2.83	0.84	
T4	6	1.20	3.00	2.25	0.79	

[a] DMBM indicates demineralized bone xenograft; PAOO, periodontally accelerated osteogenic orthodontics; PRF, platelet-rich fibrin.

Table 3 shows the means and standard deviations for the amount of extraction space in control and experimental quadrants in the PRF group (PAOO using PRF) and the DMBM group (PAOO using DMBM) at different time points (T0 to T4). Table 4 and Figure 7 illustrate the reduction in extraction space in both groups. In the PRF group, one patient did not report at T4 and one patient from the DMBM group at T3 and T4. The rate of extraction space closure of both groups, compared between maxillary and mandibular arches, showed no significant difference ($P > .05$) at various time points (T0 to T4) (Supplemental Appendix).

The rate of space closure in experimental quadrants was found to be increased in comparison to control quadrants for all time intervals (T1-T4) ($P < .05$) in the PRF group. The rate of space closure in experimental quadrants was found to be increased compared to the control quadrants at T3 and T4 [$P < .05$] in the DMBM group (Table 5). The comparative difference in the rate of extraction space closure between experimental quadrants of the PRF group and the DMBM group at different time points was not statistically significant (Table 6).

A linear mixed model with random effects was generated using both the interventions (PRF and DMBM) between the control and experimental quadrants. The random effect model is depicted in Table 7.

Comparison of mean early wound healing (EHS) scores: CSR, CSH, CSI, and Total scores between the PRF group and the DMBM group showed that only the total score of the PRF group was significantly higher than that of the DMBM group (Table 8).

Table 4. Mean Values of Extraction Space in PRF and DMBM Groups Depicting Reduction in Space Closure as Shown in Figure 7[a]

	CQ PRF	EQ PRF	CQ DMBM	EQ DMBM
T0	6.25	6.21	5.57	5.96
T1	5.5	4.64	4.81	4.7
T2	4.81	3.53	4.57	3.51
T3	4.14	2.4	4.41	2.83
T4	3.35	1.13	4	2.25

[a] CQ indicates control quadrant; DMBM, demineralized bone xenograft; EQ, experimental quadrant; PRF, platelet-rich fibrin.

DISCUSSION

PAOO combines corticotomy-facilitated orthodontics and alveolar augmentation, causing the rapid acceleratory phenomenon (RAP), thereby reducing orthodontic treatment time.[19] The advantages of graft material in PAOO include lesser limitation on pre-existing dento-alveolar volume, reduction in the need for orthognathic surgery and faster treatment time.[17,20,21] The stability of

Table 5. Inferential Statistics: Paired *t*-test for Comparison of Difference in Mean Values Between Control and Experimental Quadrants in Group 1 (PAOO Using PRF) and Group 2 (PAOO Using DMBM) at Different Time Points (T0 to T4)[a]

Group	N	Mean	SD	*P* Value
1				
T0-CQ	7	6.26	1.61	.842
T0-EQ	7	6.21	1.82	
T1-CQ	7	5.50	1.83	.036*
T1-EQ	7	4.64	1.82	
T2-CQ	7	4.81	1.75	.004*
T2-EQ	7	3.53	1.87	
T3-CQ	7	4.14	1.65	.002*
T3-EQ	7	2.40	1.62	
T4-CQ	6	3.35	1.51	.002*
T4-EQ	6	1.13	1.27	
2				
T0-CQ	7	5.57	1.90	.286
T0-EQ	7	5.96	1.39	
T1-CQ	7	4.81	1.98	.804
T1-EQ	7	4.70	1.07	
T2-CQ	7	4.57	1.86	.066
T2-EQ	7	3.51	0.95	
T3-CQ	6	4.42	1.56	.039*
T3-EQ	6	2.83	0.84	
T4-CQ	6	4.00	1.58	.015*
T4-EQ	6	2.25	0.79	

[a] CQ indicates control quadrant; DMBM, indicates demineralized bone xenograft; EQ, experimental quadrant; PAOO, periodontally accelerated osteogenic orthodontics; PRF, platelet-rich fibrin.

* $P < .05$.

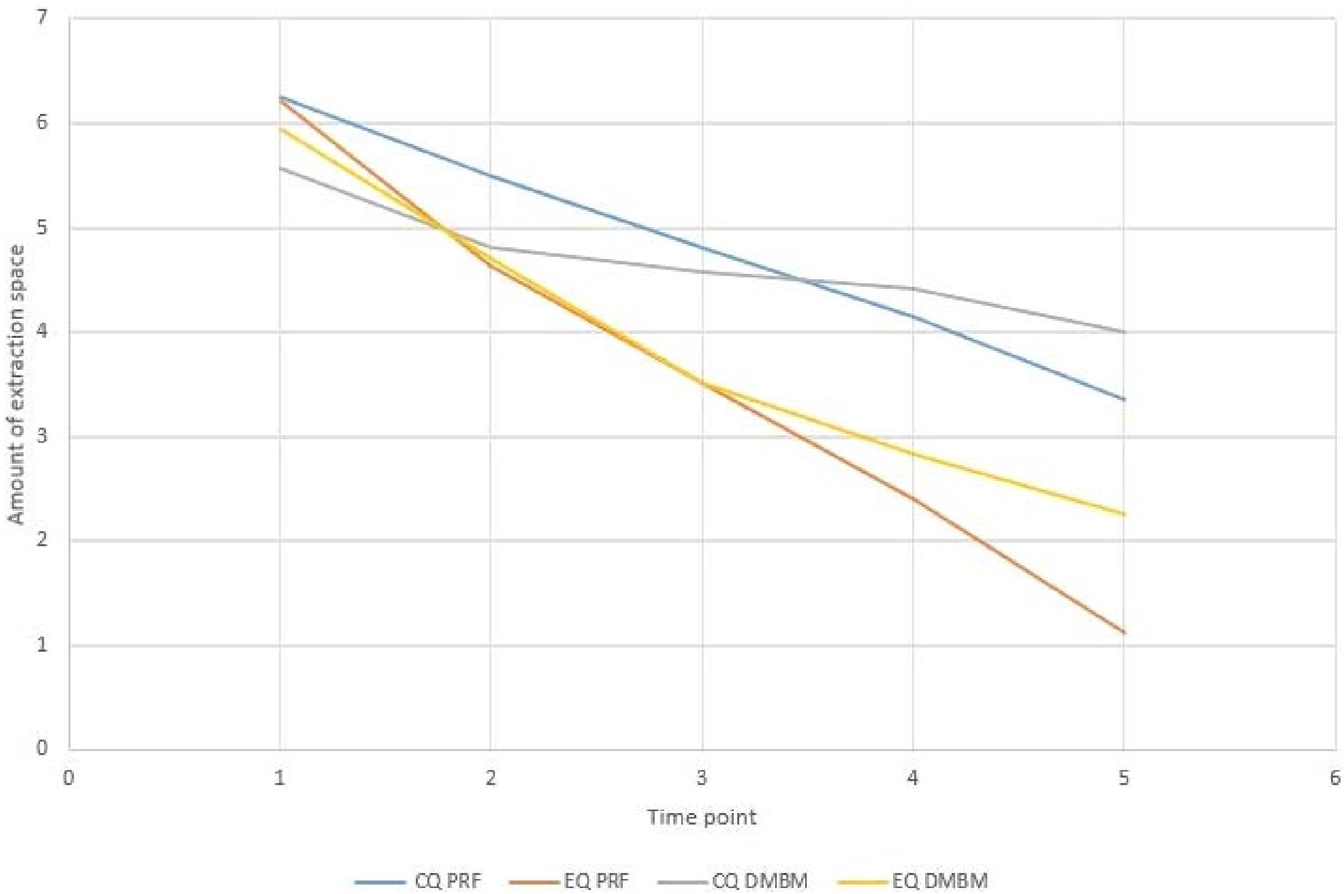

Figure 7. Illustration of reduction in extraction space in PRF and DMBM groups.

the graft incorporated during PAOO remains one of the key features to the presence of RAP throughout the period of accelerated tooth movement. Though there are various studies[22,23] that have evaluated the efficacy of less invasive procedures to accelerate orthodontic tooth movement, conventional PAOO with incorporation of graft remains more effective due to the intensity of the surgical insult to the dentoalveolar region.[24]

PRF is the platelet concentrate of an autologous bioscaffold of a dense fibrin matrix with naturally integrated growth factors. It has been shown to release growth factors over a sustained period to promote healing. A previous study comparing PRF alone or combined with freeze dried bone allograft in ridge preservation showed PRF alone was suitable for ridge preservation.[25] Accumulating evidence has demonstrated that leukocyte platelet-rich fibrin (L-PRF) releases abundant concentrations of growth factors and cytokines, accounting for a better regenerative process. Another clinical trial by Tehranchi et al.[16] compared the effect of placing PRF in extraction sockets on orthodontic tooth movement and it was observed that PRF contributed to accelerated orthodontic extraction space closure. This present study was designed as a part of an extensive clinical trial aimed at evaluating the effect of using PRF alone as graft material in the PAOO procedure.

This study did not assess the rate of canine retraction as was done in previous studies because the bracket system used was MBT, which predominantly advocates en masse space closure. Additionally, the disadvantages of individual canine retraction include additional strain on anchorage and space opening up mesial to the canine, which might be unesthetic. Mini implant supported retraction on 0.017 $\times$ 0.025-inch stainless steel wire was performed in both groups to reinforce Group A anchorage and remove the confounding factor of space closure due to anchorage loss/mesialization of the posterior segment.[26]

The rate of extraction space closure was compared between the PRF group (PAOO using PRF) vs the DMBM group (PAOO using DMBM). Both the PRF group and the DMBM group showed an increased rate of space closure in the experimental quadrants compared to control quadrants. It was observed that PAOO using PRF helped in faster extraction space closure during the initial phase of force activation. The possible regional acceleratory phenomenon started at

Table 6. Inferential Statistics (Independent *t* Test) for Comparison of Mean Values Between Group 1 (PAOO Using PRF) and Group 2 (PAOO Using DMBM) at Different Time Points (T0 to T4)[a]

Group	N	Mean	SD	*P* Value
CQ				
T0				.603
1	7	6.26	1.61	
2	7	5.57	1.90	
T1				.561
1	7	5.50	1.83	
2	7	4.81	1.98	
T2				.699
1	7	4.81	1.75	
2	7	4.57	1.86	
T3				.942
1	7	4.14	1.65	
2	6	4.42	1.56	
T4				.376
1	6	3.35	1.51	
2	6	4.00	1.58	
EQ				
T0				1.000
1	7	6.21	1.82	
2	7	5.96	1.39	
T1				.749
1	7	4.64	1.82	
2	7	4.70	1.07	
T2				.949
1	7	3.53	1.87	
2	7	3.51	0.95	
T3				.830
1	7	2.40	1.62	
2	6	2.83	0.84	
T4				.077
1	6	1.13	1.27	
2	6	2.25	0.79	

[a] CQ indicates control quadrant; DMBM, indicates demineralized bone xenograft; EQ, experimental quadrant; PAOO, periodontally accelerated osteogenic orthodontics; PRF, platelet-rich fibrin.

the 2-week time point (T1) and extended up to the 10th week (T4), whereas in PAOO using DMBM, the significance in space closure was evident at the 8th (T3) to 10th week (T4). The delay in acceleration of space closure in the DMBM group (statistically significant values evident only from T3) may possibly have been due to the osteoconductive effect of DMBM causing an increased turnover rate and the factor that bone substitutes, in general, hinder the rate of orthodontic tooth movement.[27]

Table 7. Linear Mixed Model With Random Effect[a]

Grand Mean[b]				
			95% Confidence Interval	
Mean	SE	df	Lower Bound	Upper Bound
8.819	2.307	69	4.216	13.421
7.871	2.334	69	3.216	12.527

[a] CQ indicates control quadrant.
[b] Dependent variable: CQ.

Table 8. Mann-Whitney Test for Comparison of Early Wound Healing Scores: CSR, CSH, CSI, and Total Scores Between Group 1 and Group 2[*,a]

Group	Mean Rank	Sum of Ranks	Z	Sig. (2-Tailed)
CSR			−1.140	0.254
1	8.50	59.50		
2	6.50	45.50		
CSH			−1.871	0.061
1	9.00	59.50		
2	6.00	45.50		
CSI			−0.535	0.593
1	7.93	63.00		
2	7.07	42.00		
Total			−2.014	0.044*
1	9.64	67.50		
2	5.36	37.50		

* $P < .05$ level of significance.
[a] Sig. indicates significance.

Previous studies that have used PRP have shown varying results with respect to bone turnover and orthodontic tooth movement. Since PRP has a concentration-dependent effect on bone turnover, the split mouth design of this study compensated for the intersubject variations.[28,29]

The difference in the rate of space closure in the PRF group was similar to findings of previous studies by Liou[30] and Tehranchi.[16] It was observed that the clinical effect of submucosal injection of PRP could last for 5–6 months clinically. The fastest rate of acceleration was reported to be during the second to fourth month after injection. The findings of the current study showed that the greatest difference in space closure values between the experimental and control quadrants was observed at the 8th week and the 10th week of activation of the retraction force. Clinical findings by Liou suggested that there could be an almost twofold increase in the rate of space closure with the use of repeated injection of PRP. This can be compared to the present study findings, despite that the PRF graft was placed only once prior to the start of retraction.

On comparison of early wound healing (EHS) scores between the groups, it was observed that only the mean value of the total EHS score of the PRF group was significantly higher than the DMBM group. There was no statistically significant difference in individual scores of CSR, CSH, and CSI. It was clinically observed that, in the PRF group, the incision margins were well merged and there was reduced redness along the length of the incision compared to the DMBM group.

PRF can be used as a fibrin bandage serving as scaffold to accelerate healing at wound edges. When PRF is used alone as the graft material, there is a significant acceleration in healing and this can be attributed to the fact that there is minimal foreign body reaction, which can affect the amount of bone formation.[17,31] As concurrent with the findings of this study, wound healing associated with the PAOO procedure can thus be accelerated if PRF is used as the graft material or as a membrane over the decortication area.

The limitations of this study included small sample size and an inability to randomize the patient groups. The difficulty in achieving an adequate sample size for this study can be attributed to the invasiveness of the PAOO procedure. Newer, less invasive procedures have shown accelerated orthodontic tooth movement but PAOO may always prove to be faster due to extent of the surgical injury.[22–24] Future areas of research beyond this study would include conducting a multicentric evaluation with a larger sample and evaluation of changes in the level of biomarkers associated with alveolar bone remodeling and periodontal health.

CONCLUSIONS

- Being the most effective technique in accelerated orthodontics, the graft used in periodontally accelerated osteogenic orthodontics plays an important role in influencing the rate of extraction space closure and early wound healing. Platelet-rich fibrin, due to its inherent tissue regenerative potential, can enhance the rapid acceleratory phenomenon associated with PAOO with accelerated early wound healing.

SUPPLEMENTAL DATA

The Appendix with supplemental data is available online.

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